R E M A R K S

Claims 1, 2 and 6-13 are in the application for action.

Claims 3-5 are cancelled and replaced with new claims 10-13 in order to avoid the formal issues raised by the Examiner.

Claims 1-9 are rejected under the judicially created doctrine of obviousness-type double patenting over USP 5,886,014. Reconsideration of this rejection in view of the discussion hereinbelow and other evidence that the present invention is a different invention than that described in USP 5,886,014, and patentable thereover.

The double patenting rejection over certain copending applications because of the possibility of treating cancer, is avoided by deleting the expectation of treating cancer from claim 3.

Anticipation Rejection

Claims 1-9 are rejected as being anticipated over Fujita et al. (USP 5,886,014).

Applicants respectfully submit that the presently claimed hydrochloride compound is not disclosed in USP 5,886,014.

The Examiner refers to compound 1-49 in column 29. The compound I-49 is not a hydrochloride.

The Examiner refers to column 22, lines 23-25, 36 and 37. At lines 23-25, there is reference to examples of salts with mineral acids, especially hydrohalic acids, nitric acid, perchloric acid, carbonic acid, sulfuric acid or phosphoric acid, etc. The list of numerous possibilities runs from lines 24-37. The statement of preferred which appears in lines 36 and 37, is that they be "pharmaceutically acceptable salts." Nowhere is it indicated that any one of the listed salts is preferred over another, and most of the examples in the tables are not salts.

At column 160, lines 1-37, also referred to by the Examiner, there is a description of utility and not of salts.

It is therefore submitted that there is no special indication to use chloride in the Fujita et al. document and there is no disclosure of the presently claimed hydrochloride compound. Furthermore, if one looks at all of the many examples in Fujita, by far most of the Examples refer to an acid form with a very small percentage referring to other forms.

Applicants respectfully submit that, even if it is possible to reconstruct the invention by selection of appropriate elements

from the broad general disclosure of the Fujita document, this does not place the invention in the hands of a person of ordinary skill in the art. There can be no anticipation where, without hindsight selection, the chances of discovering the invention would be the same as discovering the combination of a lock by inspection of its dials (Ex parte Garvey, 41 USPQ 583 (POBA 1939); Ex parte Starr, 44 USPQ 545 (POBA 1938)). When the claimed invention is not identically disclosed in a reference, and instead requires picking and choosing among a number of different options disclosed by the reference, then the reference does not anticipate (Akzo N.V. v. International Trade Commission, 1 USPQ 2d 1241, 1245-46 (Fed. cir. 1986), cert. denied, 107 S.Ct. 2490 (1987); In re Arkley, 172 USPQ 524, 526 (CCPA 1972).

It is therefore submitted that Fujita et al. does not anticipate the present invention as claimed.

Obviousness Rejection

Claims 1-9 are rejected under 35 USC 103(a) as being unpatentable over Fujita et al. in view of Berge et al.

Fujita et al. USP 5,886,014 is cited to reject this application as obvious, based on Fujita et al. teaching that

pharmaceutically acceptable salts, such as hydrochloric acid are preferred.

Applicants respectfully disagree.

First, there is no disclosure that hydrochloric acid is preferred in Fujita over all the many other disclosed salts described at column 22. As noted above, the disclosure at column 22 only states that "pharmaceutically acceptable" salts are preferred.

The Examiner also combines Fujita with the teaching in Berge et al. [Journal of Pharmaceutical Sciences (January 1977), Volume 66, No.1, pages 1-19] to show that the selection and preparation of the hydrochloride salt of a known compound with the expectation of improving the parent compound's properties would be obvious for one skilled in the art. Therefore, the previous Declaration is considered to be insufficient on the reasoning that the showing is not unexpected.

(To correct the record concerning said earlier Declaration, there is enclosed herewith an executed version of the earlier Declaration dated March 11, 2003 which includes the correction suggested by the Examiner in the last Office Action, i.e., on page 2 changing "Compound 3" to --Compound B--.)

Reconsideration of the rejection is respectfully requested.

There is some case that the salt form of a compound is more soluble than its free form, and also the bioactivity of the compound sometimes improves because of its increased solubility. However, Berge et al. does not specifically recommend any particular salt in general. As stated on page 1 near the end of column 1 and again at page 9 near the end of column 1, salt forms impart changed properties. However, at these portions and others throughout the Article, it is made clear that resultant salt properties depend on the salt and the compound. Thus, the effect of a salt form is not predictable in detail.

Furthermore, the bioactivity improving effect of the instant claimed compound is so strong that it would not be expected by one knowing of the increases in properties noted with respect to salt forms e.g. as from a knowledge of Berge et al. This is described below in the enclosed SECOND DECLARATION.

Therefore, even if one can reconstruct the instant claimed hydrochloride salt by hindsight reconstruction from the broad scope of the art disclosure, the invention as claimed herein is unexpected in its advantageous properties and patentable over the art.

Enclosed is a SECOND DECLARATION UNDER 37 CFR 1.132 of Kazushi ARAKI (unexecuted). An executed version is expected to be filed shortly. With reference thereto, it is noted that two kinds of additional data are presented and compared in order to explain the invention's effect more clearly: solubility and hypoglycemic activity.

In view of knowledge as discussed in the enclosed DECLARATION, it is submitted that one skilled in the art at the time of invention would expect that solubility and plasma glucose lowering rate would be directly related in the case of the compounds, which have benzylthiazolidine skeleton and insulin sensitizer action.

However, the solubility data of A (Table 2 of the SECOND DECLARATION), show there are improving effects of 2 times by salt forming. Because A and B exist as the same freeform B in the blood, if solubility becomes 2 times higher, the bioactivity should become 2 times greater.

Quite unexpectedly the activity of Compound A is not 2 times greater but rather about twenty times greater than that of its free form compound B at the plasma glucose lowering rate (Graph 2). This salt forming effect of hydrochloride salt is far greater than that which would have been expected as described in detail in the DECLARATION. Therefore one skilled in the art at

the time of the invention would not have expected this specific improving effect of the salt.

In view of above data and knowledge, the salt forming effect of instant claimed hydrochloride salt is far stronger than that would have been expected for this kind of compounds. Therefore one skilled in the art at the time of the invention would not have expected this specific effect of the salt.

In conclusion, Compound A shows an unexpected bioactivity improving effect compared to the compounds within the broad scope of the reference patent, so the invention of the hydrochloride salt claimed herein is a selection invention.

In view of the above, it is submitted that the present invention is not shown or suggested by the cited art. Withdrawal of the rejections and allowance of the application are respectfully requested.

Respectfully submitted,

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Encs. DECLARATION UNDER 37 CFR 1.132 of Kazushi ARAKI dated March 11, 2003 (Corrected)

SECOND DECLARATION UNDER 37 CFR 1.132 of Kazushi ARAKI (Unexecuted)